REMARKS

Claims 1 and 4-34 are pending in the subject application. Claims 1 and 4-13 are under examination, and rejected under 35 USC § 103.

Claim 1 has been amended to recite "wherein the host cell is adapted to grow in suspension in serum-free medium." This amendment is supported by the application at, for example, page 6, line 2 and page 9, line 24. No new matter has been added.

Claim Rejections – 35 USC § 103

Claims 1, 4-9, and 13 are rejected under 35 USC § 103(a) as being unpatentable over Gilman et al. (U.S. Patent No. 6,306,649 B1) in view of La Rosa et al. Gilman et al. is cited for teaching p65-based transcription factors in combination with a target gene construct. The Examiner states that while Gilman et al. do not specifically teach the use of p65 itself as the transcription factor in the method, La Rossa teaches that classical NF-kappa-B (p65/p50) is a potent transcriptional activator of the c-myc promoter. The Examiner asserts that it would be obvious to modify the expression method taught by Gilman et al. by using the transcription factor to be expressed in the method the p65 alone, or p65 and p50, to activate the c-myc promoter. In addition, Claims 1, 4-11, and 13 are rejected under 35 USC § 103(a) as being unpatentable over Gilman et al. and La Rosa et al. as applied to claims 1, 4-9, and 13 above, and further in view of Kushner et al. (U.S. Patent No. 5,089,397). Kushner et al. is cited for teaching that CHO cells can be maintained in protein-free medium, and are ideal hosts for recombinant protein production. The motivation alleged to combine Gilman et al. and La Rosa et al. with Kushner et al. is that Gilman et al. teach it is within the ordinary skill in the art to use mammalian cells for the expression method, and Kushner et al. teach that it is within ordinary skill in the art to use CHO cells and protein-free medium for recombinant protein expression. Thus, the Office asserts, one would be motivated to combine the references for the expected benefit of using CHO cells that are fast growing, well characterized, capable of growth in protein-free medium, and thus ideal hosts, in the expression method of Kushner.

Applicants respectfully traverse this rejection, as the cited references do not provide a motivation to combine the various aspects of the references to reach the claimed invention. The claims, as amended, are directed to an eukaryotic host cell genetically engineered to express a p65 NF-kappa-B transcription factor, and to express a protein of interest as an extracellular product, wherein the host cell is adapted to grow in suspension in serum-free medium. Gilman et al. is directed to producing cells that achieve high level expression of a target gene in genetically engineered cells, including genetically engineered cells within whole organisms (see Col. 1, lines 30-34). In particular, Gilman et al. teaches that such cells are useful in gene therapy, production of biological materials, and biological research.

However, nowhere does Gilman et al. hint or discuss engineering such cells for use in a serum-free environment, or even that such cells should be adapted to a serum-free environment. In the examples provided in Gilman et al., all of the cells transfected with the two constructs appear to have been only cultured in medium containing 10% bovine calf serum (see, for example, Col. 33, lines 32-33, lines 56-57; Col. 2, lines 55-57). Indeed, since Gilman et al.'s intention for these cells was to implant them into a host animal, one of skill in the art would be unlikely to be motivated to adapt the cells to a serum-free culture as such conditions are further removed from an *in vivo* environment in mammalian cells in which serum is present.

La Rosa et al. and Kushner et al. do not provide, either alone or in any combination with Gilman et al., the missing motivation to reach the currently claimed invention. As the Examiner notes, La Rosa et al. describe that p65 and p50, or p65 alone, activates the c-myc promoter in NIH3T3 cells. Nowhere does La Rosa et al. teach or suggest using a eukaryotic host cell genetically engineered to express a p65 NF-kappa-B factor to express a protein of interest in a serum-free culture. Instead, La Rosa et al. teaches culturing of NIH3T3 cells transfected with vectors expressing p65 in medium supplemented with 10% fetal bovine serum (see p. 1040, column 1). While Kushner et al. describes culturing a CHO cell in a serum free medium, Kushner et al. describes using a completely different type of cell, and a completely different vector (a metallothionein promoter expression plasmid) than those mentioned by either Gilman et al. or La Rosa et al. Thus one of ordinary skill would have no motivation to combine the cited references to reach the claimed invention.

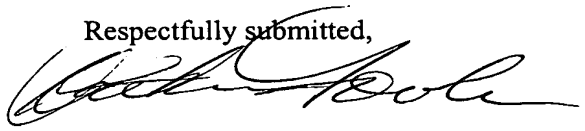
Applicants submit that the cited references would only be combined in hindsight to reach the currently claimed invention, and that a prima facie case of obviousness does not stand. Simply because an invention is within the skill of persons in the art (or those of ordinary skill) and hence enabled, is not sufficient to render the invention is obvious. The level of skill in the art cannot be relied upon to provide the suggestion to combine references. *Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308, 50 USPQ2d 1161 (Fed. Cir. 1999). In fact, the disclosure of the references tends to teach away from their combination. Applicants respectfully request that the rejections against the pending claims be reconsidered and withdrawn.

Claims 1, 4-9, and 12-13 are rejected under 35 USC § 103(a) as being unpatentable over Gilman et al. and La Rosa et al. as applied to claims 1, 4-9, and 13 above, and further in view of Levkau et al. (applicant reference C8). For the same reasons noted above, Applicants submit that the currently claimed invention is not rendered obvious by the cited art, and request reconsideration and withdrawal of this rejection as well.

CONCLUSION

An early and favorable action is earnestly requested. If any issues remain after consideration of this Amendment, the Examiner is invited to telephone the undersigned representative of the Applicants, to discuss resolution thereof.

Respectfully submitted,



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